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NVI Technology Transfer and Training Programs

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Netherlands Vaccine Institute (NVI)

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AGENDA

- Technology Transfer since 1970
  - Production Processes and QC testing
  - Generic Courses
- Training courses; future plans

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Technology Transfer since 1970
Production Processes and/or QC testing

Project	Vaccine(s)	Recipient	Country	Approach	IP-issues
Micro-carrier technology (1970-1980)	Viral vaccines	Sanofi, GSK, Sclavo (Novartis)…	Several	Turn-key	none
China Vaccine Project, World Bank (1990 – 1998)	DTP, Measles, OPV	SIBP, LIBP, KIMB, (NCL)	China	Turn-key	none
Tri-Partite Project (1997 – 2002)	DTP, TT	BioFarma, IVAC	Indonesia, Vietnam	Advice on production, QC testing and GMP aspects	none
Hib Project (1999 – now)	Hib conjugate	Bio Farma SIIL, BE Ltd Glovax/SIBP	Indonesia India Korea/China	Development and transfer of pilot process	non-exclusive license; fees and/or royalties
Combo Project (2000-2002)	DTP-HepB	Bio Farma	Indonesia	Formulation of DTP-HepB	none

Technology Transfer since 1970
Production Processes and/or QC testing

Project	Vaccine(s)	Recipient	Country	Approach	IP-issues
Animal Free Cultivation (2000 – 2003)	Viral vaccines	IPT	Tunisia	Development of a cultivation medium free from AC	none
Salk-IPV procurement (2005– now)	Salk IPV	Panacea, BE, SII, Glovax	India, Korea	Bilateral agreements Transfer of IPV related QC testing	none
ITPIV Project, WHO (2007 – now)	Egg-based inactivated influenza	VACSERA IVAC	Egypt Vietnam	1-generic, hub based 2- bilateral TT agreements	non-exclusive license; modest fees; no royalties
Sabin-IPV Project, WHO (2008 – now)	new safer polio Vaccine	T.b.d.	T.b.d.	Development and transfer of process and related QC testing	non-exclusive license; modest fees; royalties

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Micro-carrier technology

Worldwide Technology Transfer

International Symposium on Reassessment of Inactivated Poliomyelitis Vaccine. Bilthoven 1980, Develop. biol. Standard. 47, pp. 55-64 (S. Karger, Basel 1981)

Institut Mérieux, Marcy l'Etoile, F-69260 Charbonnières-les-Bains, France

THE LARGE-SCALE CULTIVATION OF VERO CELLS IN MICRO-CARRIER CULTURE FOR VIRUS VACCINE PRODUCTION PRELIMINARY RESULTS FOR KILLED POLIOVIRUS VACCINE

B.J. Montagnon, B. Fanget and A.J. Nicolas

From 1977 to 1979 we have tried to produce Killed Poliovirus Vaccine (KPV) by large-scale cultivation of primary monkey kidney cells (PMKC) in micro-carrier culture according to the methods described by van Wezel et al. (7). From fifty 140 l

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Biologicals 34 (2006) 163–166

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Production, testing and perspectives of IPV and IPV combination vaccines: GSK biologicals' view

Michel Duchêne*

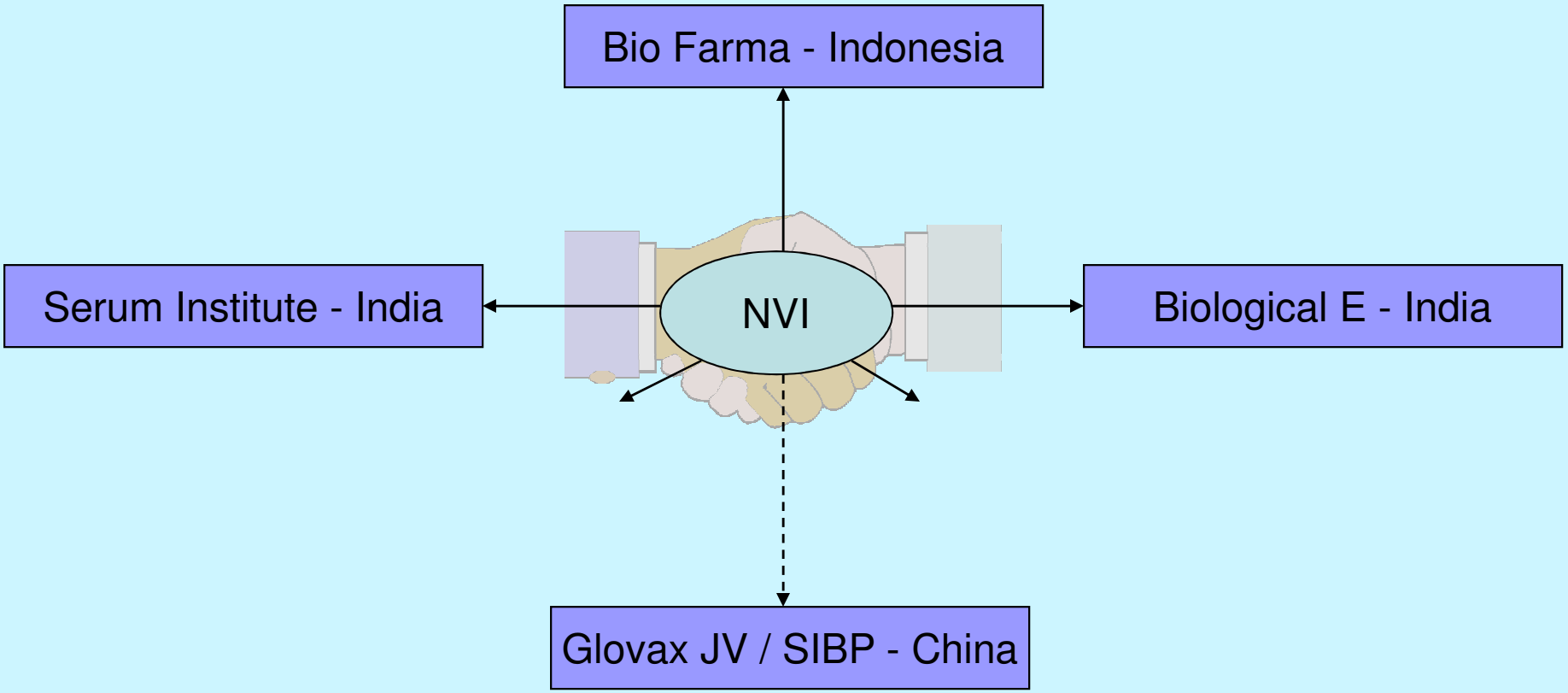
GlaxoSmithKline Biologicals, Rue de l'Institut 89, Rixensart 1330, Belgium

GSK Biologicals' current IPV is now routinely produced according to the process defined by Van Wezel (RIVM) in the late seventies, using Vero cells and micro-carrier technology in bioreactors. In addition to compliance with current requirements (World Health Organization, Euro-

Hib-conjugate vaccine project 1999 - now

- Develop an **up-scalable and patent free production process** for the large-scale production of Hib conjugate vaccine
- **Transfer the technology to developing countries** to ensure a sustainable supply of affordable and quality vaccine
- Seed capital provided by RIVM/NVI

Hib-conjugate vaccine project 1999 - now



Hib-conjugate vaccine project 1999 - now

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theHib initiative
TAKING ACTION TO PREVENT CHILDHOOD PNEUMONIA & MENINGITIS

NEWS

Serum Institute of India obtains first ever Indian license for its Hib vaccine developed through technology transfer from the Netherlands Vaccine Institute

May 3, 2007

Serum Institute of India Ltd (SII Ltd) has developed a vaccine against Hib (Haemophilus influenzae type b) and obtained a license from the Indian Government for its indigenous production. The pilot process technology know-how came from the Netherlands Vaccine Institute (NVI). This is the first time that through intensive joint development and technology transfer a developing country vaccine manufacturer successfully develops a Hib vaccine and obtains a license for it.

ITPIV, International Technology Platform for Influenza Vaccines, Project 2007 - now

- A **technology platform** for transferring a single robust production process at pilot scale with relevant documentation (SOPs, Batch Process Records, validation procedures, analytical methods and release criteria)

- A **technology package** transferable to interested developing country vaccine manufacturers, upon request and without IPR hurdles

- Selected technology: **Inactivated whole virion influenza vaccine produced in embryonated eggs >>> extended to split and in the future to cell-culture derived vaccine**

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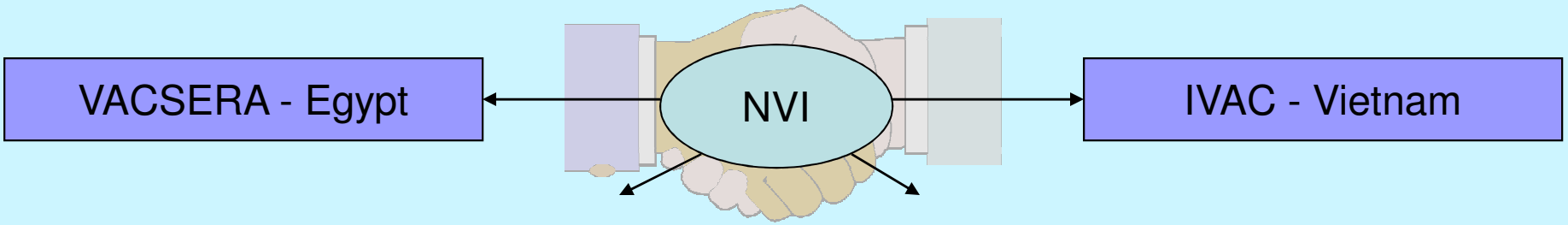
Training courses realised 2009/2010

- Generic courses
  - **3-week courses on influenza production and QC**
  - **Up to now 29 trainees**
- Workshop
  - **1-week workshop on QA and GMP aspects of influenza vaccine production**
  - **13 participants**

DCVMs participating in NVI Flu Courses

Country	Benificiary	Legal Status
Argentina	Centro Nacional de Control de Calidad de Biológicos	Public
China	Shanghai Institute of Biological Products	Public
China	Changchun institute of Biological Products	Public
China	ZhejiangTianyuan Bio-pharmaceutical	Private
Croatia	Institute of Immunology	Public
Egypt	Vacsera	Public
India	Indian Immunologicals Limited	Private
Indonesia	Bio Farma	Public
Iran	Razi	Public
Kazakhstan	Research Institute for Biological Safety Problems	Public
Romania	Cantacuzino	Public
Serbia	Torlak	Public
Thailand	GPO	Public
Thailand	Thai Red Cross Society	Public
Vietnam	Ivac	Public

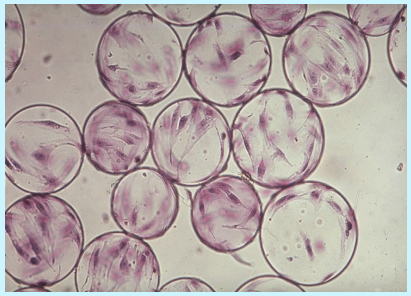
ITPIV, International Technology Platform for Influenza Vaccines, Project 2007 - now



Establishment of Hub for flu successful as capacity-building tool

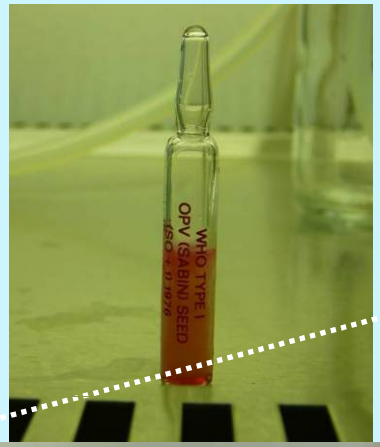
- Egg-based process development:
  - **Consistent process**
  - **Meeting industrial standards for yield**
  - **Meeting all international specifications**
  - **Suitable for technology transfer**
- Training & Tech Transfer
  - **Generic training meets international need**
  - **Alternative way in addition to stepwise approach starting with fill/finish**
- Work to be started on transferable vero-cell based flu process

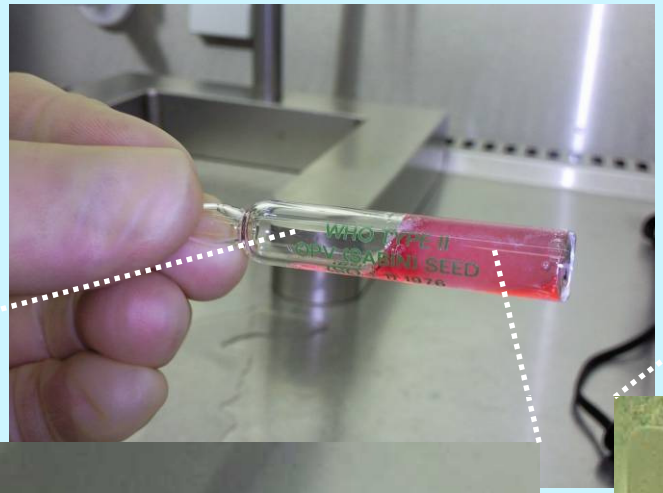
Sabin-IPV vaccine project 2008 - now

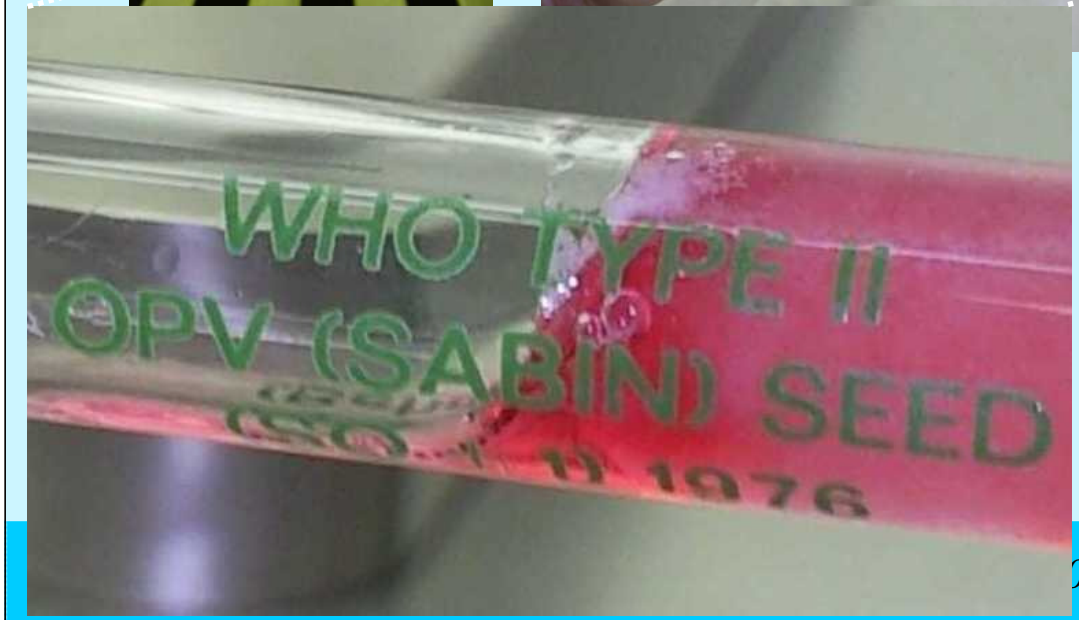


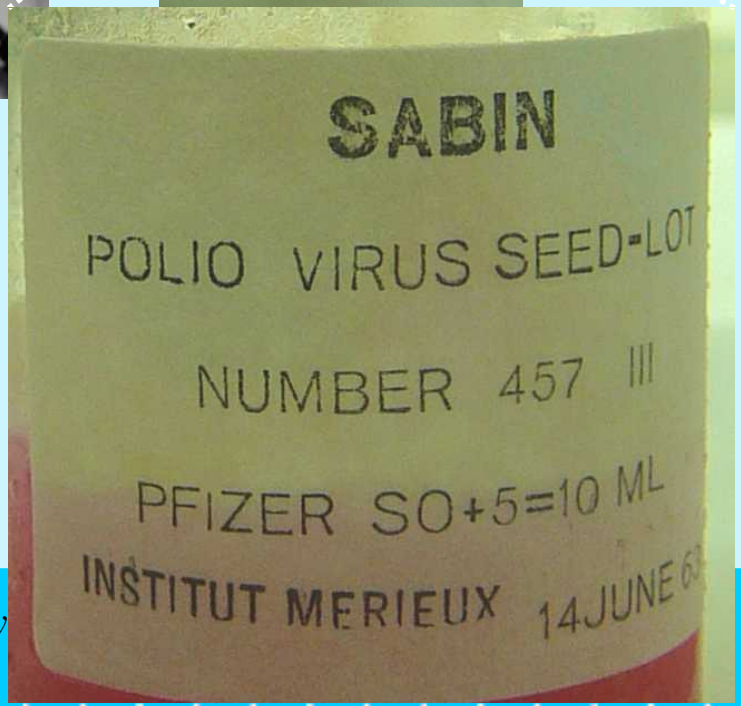
- Sabin-IPV based on NVI Salk-IPV Vero/ micocarrier technology
- Production of Master/ Working seedlot
- Preparation of clinical lots and process fine-tuning/ optimization
- (Pre)clinical and phase I clinical studies
- Technology Transfer to potential partners
- Financed partly by WHO

Sabin-IPV vaccine project
2008 – now
Master (3x) & Working (3x) Seedlots prepared









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Future Plans
Training Courses 2011/ 2012

- 3 week generic egg-based course, whole cell and split (2011)
- 4 week generic conjugate course (2011)
- 1 week workshop on QA and GMP aspects (2011)
- 1 week workshop on Master and Seed Banking, mainly influenza (2011)
- Develop Vero cell technology training
- Run a 4 week Vero cell technology training (2012)
- Develop web-based support forum for courses, to allow follow-up activities and give access to update course documents

Pending availability international funds…..

Future Plans
Collaboration with UNIL, Lausanne

- University of Lausanne (UNIL) is a WHO technology transfer 'hub' on adjuvants.

- **NVI and UNIL signed in 2010 a Letter of Intent to collaborate on**
  - IPV in the context of dose sparing approaches using adjuvants
  - Adjuvanted pandemic influenza vaccine transfer to DCVMs.
  - Collaborative training in vaccine formulation particularly in the fields of pandemic Influenza and Sabin-IPV

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Thank You

- Technology Transfer of **Hib conjugate vaccine(Beurret & van der Put)**
- Technology Transfer of **egg based Influenza vaccine (de Boer & Luytjes)**
- Technology Transfer of **Sabin-IPV (Bakker & van den Heuvel)**

Jan Hendriks
Ahd Hamidi
Marit Holleman

Websites:

www.NVI-vaccin.nl

www.Sabin-IPV.nl

www.ltpiv.nl